REMARKS

Independent claims 1 and 140 have been amended to further highlight their patentability over the prior art of record. Dependent claims 3, 6, 40 and 143 have also been amended. Claims 5 and 142 were previously canceled, and claims 42-139 previously withdrawn.. Dependent claims 2, 4, 7-39, 41 and 141 remain unchanged. Applicants also present arguments below in further support of the patentability of all claims in view of the rejections set forth in the pending Office Action.

Claims 1-4, 6-41, 140, 141 And 143 Stand Rejected Under 35 U.S.C. §103(a)

Claims 1-4, 6-41, 141 & 143 stand rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent 6,468,506 to *Rŏssling et al.* in view of U.S. Patent 5,885,216 to *Evans, III et al.* and further in view of U.S. Patent 6,231,513 to *Daum et al.* or International Pub. WO96/40282 to *Quay et al.*

Applicants respectfully believe that such a conclusion is incorrect even before consideration of the amendments herein. Nevertheless, Applicants have amended the claims to more definitively set forth the subject matter they wish to claim. In particular, Applicants have amended independent claims 1 and 140 to include an imaging unit that, in conjunction with the reservoir, pressurizing device, bubble generator and controller, forms a system novel and unobvious over the cited prior art.

As amended, claim 1 is now directed to a system for creation and adjustment of a bubble medium for real time administration into a patient. In addition to the imaging unit that enables "*an operator to image a region of the patient into whom the medium is being injected and thus monitor the effect of the medium therein*," the claim recites a "*a controller* [that has] *a user interface for enabling the operator to adjust in real time at least one operating parameter of said system pertaining to generation and/or delivery into the patient of the medium inclusive of properties of the bubbles therein for the purpose of at least one of stabilizing and optimizing a medical procedure being performed on the patient.*" Consequently, these amendments make it clear that the bubble medium is generated for

real time administration into the patient so as to optimize according to the demands of the operator a medical procedure being performed on the patient.

The prior art cited in the Office Action neither individually nor collectively teach or even suggest such a system. More specifically, the systems and apparatuses of the prior art are in no way directed to a system whose controller is capable of real time control of the properties of the bubbles in a medium that is being prepared for real time administration into a patient.

The *Rŏssling et al.* patent only teaches the making of dried microparticles to which water is to be added later for purpose of re-hydrating to create a bubble-based contrast medium. It discloses a method of making dried spherically-shaped microparticles in which a gas (e.g., air) is enclosed. (col. 2, lines 1-2; col. 9, line 65) The last step of the method involves removing the dried microparticles from column 19, as shown in Figure 1. (col. 5, lines 28-33; col. 10, lines 32-36) Even before this step in the process, the properties of the gas-filled microparticles has become unalterable. (col. 5, lines 28-33) Properties such as the size of the microparticles, the type of gas enclosed in the microparticles, the composition of the shell of the microparticles, etc, are set and cannot be changed on the fly. The dried micro-particulate product is destined only for packaging and shipment for later use at sites where ultrasound imaging procedures can be performed. Once delivered to such a site, the dried particles can then be suspended in a pharmaceutically acceptable suspension medium (e.g., water) to create the contrast agent. (col. 3, lines 60-67) Unlike Applicants' claims, the *Rŏssling et al.* patent thus does not disclose a system whose controller enables an operator to "*adjust in real time* [the] *parameter*[s] … *pertaining to generation and/or injection of the medium* ***inclusive of the properties of the bubbles therein***" for the purpose stabilizing and/or optimizing a medical (e.g., imaging) procedure being performed on the patient. Nor does *Rŏssling et al.* teach such a controller as part of a system having an

imaging unit from which images can obtained to further enable the operator to make real time adjustments in the medium to optimize the medical procedure being performed.

Despite the foregoing, the Office Action in section 14 attempts to give relevance to the `506 patent by stating that "*Rossling et al.* does not exclude a controller, such as a human who is capable of real time control of the properties of the bubbles...." Such relevance is undeserved, however. The act of not excluding information about a device can met by any patent, technical paper or other publication that fails to disclose such information or is completely silent about it in the first place. As it would be for patents on children's toys so it is with the *Rŏssling et al.* patent.

And, as for the assertion that *Rŏssling et al.* teaches "real time control of the properties of the bubbles," this is unsupported by the text and drawings of that reference. As amended, claim 1 of the present application recites a "*controller ... for enabling the operator to adjust in real time* [the] *parameter*[s] *... pertaining to generation ... of the medium* ***inclusive of properties of the bubbles therein***...." The size of the dried gas-filled microparticles created by the method of *Rŏssling et al.* is entirely dependent on the nozzle --its size, shape and type -used in their manufacture. (column 3, lines 49-51) As noted above, properties such as the size of the particles, the type of gas enclosed in the particles, the composition of the shell of the particles, etc, are set and cannot be changed on the fly. (col. 5, lines 28-33) The dried micro-particulate product is destined only for shipment for later use.

Similarly, the *Evans, III et al.* patent, either alone or in combination with the *Rŏssling et al.* patent, also does not teach the system recited in claim 1. Instead, it discloses a process/system that permits contrast of varying concentration to be injected into a patient. The bottom line is that the *Evans, III et al.* patent teaches only the mixing of contrast to the desired concentration and delivery of same into the patient. (col. 5, lines 60-61; col. 6, lines 38-40)

While the *Evans, III et al.* patent discloses a system for diluting contrast to a desired concentration level and administering same into a patient, it teaches nothing about "*creation and adjustment of a bubble medium for real time administration into a patient*," as is recited in claims 1 and 140. The ability to "*adjust in real time* [the] *parameter*[s] *... pertaining to generation ... of the medium* ***inclusive of properties of the bubbles therein***" coupled with "***real time administration into a patient***...," as recited in claims 1 and 140, is not disclosed by *Evans, III et al.*

If the teaching of *Rŏssling et al.* could be combined with those of *Evans, III et al.*, it would certainly not yield a contrast dilution system in which the properties of the bubbles could be created and adjusted real time and then administered immediately into a patient. This is because, for example, any such change in microparticle size would require a different nozzle to be installed in the apparatus of *Rŏssling et al.*, as noted above, which Figure 1 suggests is an arduous and time-consuming task -- a manual task that is contrary to the real-time adjustment of bubble properties real time administration of the medium of Applicants' claims. In this regard, *Evans, III et al.* in fact teach away from what the Applicants have claimed in the present application.

The *Daum et al.* and *Quay et al.* references are likewise inapposite to buttress the pending 35 U.S.C. §103(a) rejection.

The *Daum et al.* patent discloses devices that are inserted into a blood vessel wherein they are used to form microbubbles in the blood for use in ultrasonic imaging procedures. One such device is a needle 20 in whose pointed distal end 21 is housed a beveled porous matrix 23. When the needle 20 is inserted into a vessel, gas passes through the lumen 24 and flows through the porous matrix 23 resulting in the formation of microbubbles in the blood. (col. 3, lines 57-63) Another such device features a needle 101 at the proximal end 103 of which is affixed a piezoelectric ultrasound transmitter 102. In operation, the distal end of needle 101 is inserted into a vessel. Gas from a source thereof then flows via connector 105 through the hollow shaft of needle 101 and into the vessel. While that is happening,

ultrasonic waves formed by activation of transmitter 102 causes vibrations that break the flow of the gas into microbubbles within the blood stream. (col. 4, lines 10-23)

The *Quay et al.* publication discloses a method/apparatus for forming a "microbubble-containing solution" and then administering that solution to an animal. (p. 22,lines 4-8; p. 23, lines 1-5 & 13-15) The solution is formed only in bulk volume (Id. & p. 8, lines 6-25), i.e., all at one time, and it is formed using an activation method, which *Quay et al.* expressly define as only through the use of "a hypobaric force on [the] solution." (p. 5, line 36 - p. 6, line 3) In other words, the apparatus of *Quay et al.* creates bubble-based media only in bulk volume and only in response to the lowering of pressure in the container in which the solution is stored. Consequently, unlike the system recited in the pending claims, the apparatus of *Quay et al.* is not capable of creating, and hence altering the characteristics of, the bubbles on the fly, as the demands of the medical procedure change. The real-time control of Applicants' claimed system over the bubble generator recited in the claims makes this possible.

The *Daum et al.* patent pertains only to creation of bubbles directly within a blood vessel by means of gas injected via a needle. The *Quay et al.* publication pertains only to bulk formation of a bubble contrast medium, which is then injected into the blood stream. Neither reference discloses a system whose a controller permits an operator to change/control real time the properties of the bubbles in the medium, which is, for example, then promptly administered into a patient.

Finally, even if the teachings of *Rŏssling et al.* could be combined with those of *Evans, III et al.*, at best they would yield a contrast dilution system to which the dried microparticles of *Rŏssling et al.* would somehow be added. This mixture might result in a diluted bubble contrast medium but one in which the size and other characteristics of the bubbles are all the same. The system of independent claims 1 and 140 and their respective dependents, however, permit production of a medium in which the properties of the bubbles and the overall medium can be varied real time. Claim 6 recites some of the properties that can be changed on the fly, e.g., the composition of the medium, the composition of

the bubbles in the medium, the concentration of the bubbles in the medium, the size of the bubbles in the medium, the rate of flow of the medium, the volume of the medium administered, the timing of the administration of the medium, the sequencing of the administration of the medium, the pressure of the medium and the temperature of the medium can all be controlled real time according to the demands of the operator during a medical procedure (e.g., an imaging procedure).

For the above reasons, Applicants respectfully submit that combined teachings of *Rŏssling et al.*, *Evans, III et al.* and *Daum et al.* or *Quay et al.* do not render obvious the subject matter recited in independent claims 1 and 140 and their dependents 2-4 & 6-41 and 141& 143, respectively. In view of the foregoing amendments and arguments, Applicants believe that the §103(a) rejections have been overcome.

Claim 40 Stands Rejected Under 35 U.S.C. §112, Second Paragraph

Claim 40 stands rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In section 25 of the Office Action, the Examiner states that:

> The recitation of a "first member and second member" is confusing and unclear as there are no structural properties for the first and second members provided in the disclosure.

Applicants believe that they have amended claim 40 to overcome this rejection.

Although various claims have been amended or canceled during prosecution, Applicants wish to point out that such revisions are not meant to be construed as an admission of unpatentability of the subject matter recited in earlier versions of the claims. Instead, such revisions should be considered as having been made only to expedite prosecution of the application. They should not be considered as a surrender of the right to pursue any subject matter disclosed in the present application or in any continuation or divisional application based thereon that may be filed in the future.

CONCLUSION

Before entry of this *Amendment And Response*, the present application had forty-three (43) claims pending, two (2) of which independent. Upon entry of this *Amendment And Response*, the number of claims remains unchanged though several have been amended. Earlier in prosecution, ninety eight (98) claims were withdrawn with traverse due to an restriction requirement.

Given the foregoing amendments and arguments, Applicants respectfully request withdrawal of the rejections set forth in the Office Action dated 30 April 2009. Applicants believe the application is ready to be allowed. If the Examiner has any questions regarding this *Amendment and Response*, he is invited to call the undersigned at the telephone number listed below.

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Respectfully submitted,

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